REMARKS

In this communication, Applicants have canceled Claims 40-42 and added new Claims 43-68. The new claims are supported by the specification as filed and the original claims. No new matter is introduced. Claims 1-39 and 43-68 are pending. Applicants would like to take this opportunity to thank Examiner Akhavan for conducing a telephone interview with Applicants' representative to discuss the scope of the claims. Allowance of all pending claims is respectfully requested.

Rejection under 35 U.S.C. § 112, First Paragraph

(1) Written description

Claims 33, 34, 37 and 39-42 stand rejected under 35 USC § 112, first paragraph, as allegedly failing to comply with the written description requirement for reasons stated on pages 4-7 of the Office Action. Applicants respectfully traverse this rejection.

According to the Federal Circuit in Enzo Biochem, Inc. v. Gen-Probe Inc., compliance with the written description requirement is essentially a fact-based inquiry that will necessarily vary depending on the nature of the invention claimed. Enzo Biochem, Inc. v. Gen-Probe Inc. 63 USPQ2d 1609, 1616 (Fed. Cir. 2002). The written description requirement is satisfied by the patentee's disclosure of "such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." Id at 1620 citing Lockwood v. American Airlines, Inc. 41 USPQ2d 1961, 1966 (Fed. Cir. 1997) .

Independent Claim 33 is directed to a method for introducing a substance into cells using the compound described in Claim 1. The method comprises the steps of (1) forming a liposome from a compound as set forth in Claim 1; (2) contacting the liposome with the substance to form a complex between the liposome and the substance; and (3) incubating the complex with one or more cells.

Applicants respectfully submit that the compound of Claim 1 is properly described in the specification. The chemical formula of Claim 1 is commonly used in the chemistry art to represent a group of chemical compounds that share a common feature or features. Similar formulas have been widely used in publications, patents, and patent applications (see e.g., U.S. Patent Nos. 6,300,321 and 6,610,664).

Applicants further submit that the three steps recited in Claim 33 are also properly supported by the specification. With respect to the step of forming a liposome, it is well known to one skilled in the art that the formula of Claim 1 represents a general structure of certain cationic lipids, and that all cationic lipids share certain common features, such as being positively charged under neutral pH and having the ability to form liposome structures in an aqueous environment under agitation. The methods of forming liposomes were well known in the art at the time the application was filed (see, for example, U.S. Patent Nos. 4,897,355 and 5,171,678, both are cited in the specification).

With respect to steps 2 and 3, it was well-known to one skilled in the art at the time the application was filed that cationic lipid compounds are capable of delivery of macromolecules, such as DNA, RNA, protein, and small chemical compounds into cells. As described in the specification and in the cited references, lipid aggregates comprising cationic lipid components have been shown to be especially effective for delivering anionic molecules into cells. Typically, the lipid aggregates (e.g. liposomes) form complexes with the anionic molecules. When incubated with cells, the complexes fuse with the cell membrane and introduce the molecules into the cells. The incubation conditions were also well known in the art at the time the application was filed (see, for example, U.S. Patent Nos. 4,897,355 and 5,171,678, both are cited in the specification).

Accordingly, Applicants respectfully submit that the specification conveys with reasonable clarity to one skilled in the art the method set forth in Claim 33.

Dependent Claim 34 limits the substance of Claim 33 to a nucleic acid, an oligonucleotide or a carbohydrate. Dependent Claim 37 recites that the compound of Claim 33 is associated with a pharmacological agent or a genetic material. Dependent Claim 39 recites that the compound of Claim 37 is associated with a genetic material selected from the group consisting of DNA, RNA, oligonucleotides, and nucleic acids. Applicants respectfully submit that all the additional limitations in the dependent claims were well known in the art at the time when the application was filed, and that the specification provides with reasonable clarity to one skilled in the art a description of the invention defined by the claims.

The Office Action asserts that "[a]lthough the specification appears to present some species (e.g. Drawings, Figs. 7-11), there is no relative teachings as to whether the lipid structures presented actually effectuate transfer of genetic material into cell.

Applicants respectfully submit that the delivery mechanism of lipid aggregates (e.g., liposomes) is based on the electrostatic interaction between the positively charged cationic lipid molecules and the negatively charged anionic molecules, and the lipid-lipid interaction between the lipid-anionic molecule complex and cell membrane. One skilled in the art understands that any cationic lipid having the general structure of formula (I) is capable of binding to an anionic molecule, fusing with a cell membrane, and introducing the anionic molecule into the cell, which is all that is required to practice the methods of Claims 33, 34, 37 and 39.

The Office Action also alleges that "due to various substitutions of attached to different points in the chemical formula presented, there is an enormous number of different combinations that can result, each with a distinct chemical formula with attendant effects with respect to, for example, **transfection efficiency, serum compatibility or targeting**." Applicants respectfully submit that this rejection is based in part upon an improper interpretation of exactly what is Applicants' invention.

Although transfection efficiency may vary depending on the chemical structure of the lipid, the characteristics of the anionic molecule of interest, the type of cells to be transfected, and a number of other factors, it is not part of the claimed invention. Since Claims 33, 34, 37 and 39 do not recite a specific efficacy, there is no requirement for providing a written description on the transcription efficiency. In addition, optimization of transfection conditions is routinely performed in the art and is generally part of a standard transfection protocol. For example, see Ausubel et al. Short Protocols in Molecular Biology, 2nd Edition, Section 9.4: Liposome-Mediated Transfection and Section 9.9: Optimization of Transfection; and Promega Inc.'s Transfection Guide, Chapters 1-3, both of which were available to one skilled in the art before the filing date of the instant application.

Taken together, Applicants respectfully submit that the specification provides proper written description for Claims 33, 34, 37 and 39. Withdrawal of the 35 U.S.C. § 112, first paragraph, reject for lack of written description is respectfully requested. Applicants further submit that, based on the same reasoning discussed above, the specification also provides proper written description for new Claims 43-68.

Claims 40-42 have been canceled by this communication. Rejection to these claims are now moot.

(2) Enablement

Claims 33-34, 37 and 39-42 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement for reasons stated on pages 7-11 of the Office Action. Applicants respectfully traverse this rejection.

As discussed by the Examiner in the Office Action, there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary

experimentation is "undue." In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors are addressed below.

Scope/Breadth of the claims: The claims are directed to methods of introducing a substance (e.g., a genetic material) into cells via lipid aggregates such as liposomes.

The nature of the invention: The invention involves the transfer of a substance (e.g., a genetic materia) into cells both *in vitro* and *in vivo* using cationic lipid aggregates.

The state of the prior art: Cationic lipids have been widely used to introduce genetic material into cells in both *in vitro* and *in vivo* settings. It is well-known in the art that the lipids may form liposomes or other types of lipid aggregates which are capable of forming complexes with negatively charged substances, such as proteins and polynucleotides. When bought into contact with a cell surface, the complexes fuse with cellular membranes through a mechanism that implicates both lipid-lipid interactions and endocytosis, and bring the negative charged substances into the cell. This process is often referred to as "transfection." As discussed earlier, although the efficiency of transfection may vary depending on the structure of the lipid, the characteristics of the negatively charged substance, and the type of cells to be targeted, one skilled in the art would understand that any cationic lipid, by nature, is capable of forming a complex with a negatively charged substance and fusing with a cell membrane to introduce the substance into the cell.

The level of one of ordinary skill in the art: The level of one of ordinary skill in the art is high in the field of biotechnology. Typically, a person practicing the instant invention would have a Ph.D. degree in biochemistry, molecular biology or a related field, and have one or more years of post-doctorate experience.

Amount of guidance provided: The specification teaches that the lipid aggregates according to the invention can be used as transfection agents for the delivery of DNA, RNA, oligonucleotides, peptides, proteins, carbohydrates and drugs into cells. It also teaches that the

lipid aggregates can be formed using a lipid aggregate forming compound such as DOPE, DOPC or cholesterol, and that the compounds according to the invention may also be mixed with other substances such as proteins, peptides and growth factors to enhance cell targeting, uptake, internalization, nuclear targeting and expression. (Page 19, lines 14-24). As stated in the specification, methods of transfection and delivery of lipid aggregates are well-known in the art. The specification has also incorporated by reference a number of U.S. patents and publications detailing the preparation of lipid aggregates and methods of transfection in both *in vitro* and *in vivo* settings. (See e.g., page 3, lines 8-10; page 4, lines 4-6; and page 21, line 15).

Number of working examples: The specification does not contain any working examples. Applicants, however, have enclosed a 1.132 Declaration demonstrating that the claimed compounds are indeed capable of introducing DNA and siRNA into cells using the claimed method.

Amount of Experimentation required. In order to practice the claimed invention, one would need to form a lipid aggregate (Claim 68) or a liposome (Claim 33) comprising a lipid of the instant invention, incubating the lipid aggregate or liposome with a substance of interest to form a complex, and incubating the complex with one or more cells. The standard conditions for these procedures are well known to one skilled in the art. For example, U.S. Patent Nos. 4,229,360; 4,224,179; 4,241,046; 4,078,052; 4,235,871; 4,897,355; and 5,171,678, which are incorporated by reference, provide a variety of liposome formulations. As detailed in the working examples provided in the attached Declaration, the lipids of the instant invention can be used to introduce foreign substance into cells under standard experimental conditions. The working examples clearly demonstrate that no undue experimentation is required to practice the method of the instant invention.

Taken together, Applicants respectfully submit that the instant application contains sufficient information to enable one skilled in the art to make and use the invention recited in

Claims 33, 34, 37 and 39 without undue experimentation. Withdrawal of the 35 U.S.C. §112, first paragraph, rejection for lack of enablement is respectfully requested. Applicants further submit that, based on the same reasoning discussed above, new Claims 43-68 are properly enabled by the specification.

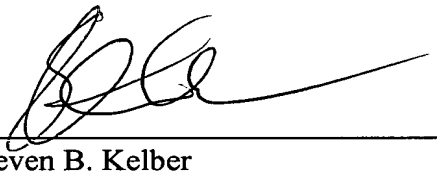
Claims 40-42 have been canceled by this communication. Rejection to these claims are now moot.

CONCLUSION

In view of the foregoing remarks, favorable reconsideration of all pending claims is requested. Applicants respectfully submit that this application is in condition for allowance and requests that a notice of allowance be issued. Should the Examiner believe that anything further is required to expedite the prosecution of this application or further clarify the issues, the Examiner is requested to contact Applicants' representative at the telephone number listed below.

Respectfully submitted,

PIPER RUDNICK LLP



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